REMARKS

Applicants thank the Examiner for the review of the instant application. Applicants acknowledge the Examiner's withdrawal of the rejection of the pending claims under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, as lacking utility and enablement.

Applicants have amended claim 1 to delete "amino acids 34-321 of" as suggested by the Examiner in a telephone interview on May 7, 2007 and May 9, 2007. Applicants have added new claims 7-11. Support for these claims can be found throughout the application as filed, for example at paragraphs [0035]-[0036] and Table 7.

Claims 1-5 and 7-11 are presented for examination. Applicants respond below to the specific rejections raised by the Examiner in the pending Office Action. For the reasons set forth below, Applicants respectfully traverse.

Rejections under 35 U.S.C. § 112, first paragraph – Written Description, New Matter

The Examiner has rejected pending Claims 1-5 under 35 U.S.C. §112, first paragraph, as containing new matter. *Office Action* at 3-4. Specifically, the Examiner objects to claim limitations related to amino acids 34-321 of SEQ ID NO:10. Applicants respectfully traverse.

Applicants maintain that the objected to matter is supported by the specification as filed. However, solely in the interest of advancing prosecution, Applicants have deleted "amino acids 34-321 of" from claim 1, rendering the rejection moot.

Sequence Rule Compliance

The Examiner states that the application fails to comply with the requirements of 37 C.F.R. § 1.821(a)(1) and (a)(2), and requests that a paper copy of the sequence listing be replaced.

In response to the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures, a copy of which Notice is enclosed, Applicants request amendment of the specification to include the sequence listing, a paper copy of which is submitted herewith. Pursuant to 37 C.F.R. § 1.821(f) and (g), Applicants state that the sequence listing information recorded in computer readable form filed with the application is identical to the written sequence listing submitted herewith, and that no new matter is added.

35 U.S.C. § 102(b) – Baker *et al.*

The Examiner has rejected claims 1-5 under 35 U.S.C. § 102(b) as being anticipated by Baker (WO 99/63088). The Examiner states that the limitation "amino acids 34-321 of SEQ ID NO:10" is not supported by the original disclosure and constitutes new matter, and that the 35 U.S.C. § 102(b) rejection is based on an effective filing date of May 1, 2002, the filing date of the present application.

To be anticipated under 35 U.S.C. § 102(b), the invention must be patented or described in a printed publication "more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b). Applicants submit that Baker *et al.* does not anticipate any of the pending claims under 35 U.S.C. § 102(b) because it was not published more than one year prior to the date of the instant application for patent in the United States.

The instant application is a continuation of, and claims priority under 35 U.S.C. § 120 to, US Application 10/006867 filed 12/6/2001, which is a continuation of, and claims priority under 35 U.S.C. § 120 to, PCT Application PCT/US00/23328 filed 8/24/2000. The data in Example 18 (Tumor Versus Normal Differential Tissue Expression Distribution), relied on in part for the utility of the claimed antibodies are disclosed in PCT Application PCT/US00/23328 filed 8/24/2000, on page 93, line 3, through page 96, line 35. To the extent that the Examiner rejected the priority claims based on recitation of "amino acids 34-321 of SEQ ID NO:10," Applicants note that they have deleted this limitation. Therefore, the instant application is entitled to a priority date of at least August 24, 2000.

Baker *et al.* was published December 12, 1999, which is not more than one year prior to August 24, 2000, and therefore Baker *et al.* is not prior art under 35 U.S.C. § 102(b). Applicants request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 102(b) based on Baker *et al.*

35 U.S.C. § 102(e) – Afar *et al.*

The Examiner has rejected claims 1-5 under 35 U.S.C. § 102(e) over Afar *et al.* (U.S. Pub. No. 2005/0019870). The Examiner states that Afar discloses a prostate tumor associated gene (24P4C12) and its encoded protein. The Examiner asserts that the 24P4C12 protein, which is 710 amino acids long, is identical to amino acids 34-321 of SEQ ID NO: 10. The Examiner

states that Afar discloses and claims anti-24P4C12 antibodies. The Examiner states that regions of the 24P4C12 protein that show immunogenic structure as well as other regions and domains can be identified using methods known in the art, including Kyte-Doolittle. The Examiner presents a Kyte-Doolittle plot of 24P4C12. The Examiner argues that "[a]nti-24P4C12 antibodies that specifically bind epitopes in the 398-710 amino acid region of 24P4C12 will also specifically bind SEQ ID NO: 10 because this region of 24P4C12 is identical to amino acids 34-321 of SEQ ID NO: 10. Applicant has the burden of distinguishing between anti-24P4C12 antibodies and the claimed antibodies." *Office Action* at 8. Applicants respectfully traverse.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Claim 1 recites: "An isolated antibody that specifically binds to the polypeptide having the amino acid sequence of SEQ ID NO: 10." According to the Examiner, Afar discloses antibodies to a protein sequence that is 710 amino acids long – 379 amino acids longer than SEQ ID NO:10. Therefore the Afar reference does not expressly disclose an antibody which specifically binds to the polypeptide of SEQ ID NO:10, since the majority of 24P4C12 does not correspond to SEQ ID NO:10. Because Afar does not expressly disclose the claimed subject matter, Afar can anticipate the pending claims only if it inherently discloses an antibody that satisfies this claim. The M.P.E.P. states that:

> To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is **necessarily** present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, **may not be established by probabilities or possibilities**. The mere fact that a certain thing **may** result from a given set of circumstances **is not sufficient**." *M.P.E.P.* §2112 ¶IV (8th ed. 2004), quoting *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (emphasis added).

Given the above standard, the Afar reference inherently anticipates the claimed invention only if the answer to the following question is "yes":

> Does an antibody raised against 24P4C12 of Afar necessarily, always and without exception, possess the property of specifically binding to the polypeptide of SEQ ID NO:10?

Applicants assert that the answer to this questions is clearly "No."

According to the Examiner's sequence alignment on page 7 of the Office Action, amino acids 398-710 of 24P4C12 disclosed in Afar are identical to amino acids 9-321 of SEQ ID

NO:10. Applicants note that amino acids 390-397 of Afar are not the same as amino acids 1-8 of SEQ ID NO:10. The Examiner has not established that there is any similarity between amino acids 1-397 of Afar and SEQ ID NO:10. Therefore, according to the Examiner's alignment, 397 of the 710 amino acids of 24P4C12 are apparently completely different from SEQ ID NO:10. That means that 56% of 24P4C12 differs from SEQ ID NO:10. Those of skill in the art recognize that as little as a single amino acid change can destroy binding specificity of an antibody to a target. *See, e.g., Peerlink et al.*, Blood, 1999; 93:2267-73 (teaching that plasma or polyclonal IgG inhibited wild-type factor VIII activity, but not the activity of factor VIII having a single amino acid mutation) (Abstract attached as Exhibit 1); *Deregt et al.*, Virus Res., 1998; 53:81-90 (teaching that single amino acid changes were sufficient to destroy binding of monoclonal antibody to target protein) (Abstract attached as Exhibit 2); *McGuinness et al.*, Mol. Microbiol., 1993; 7:505-14 (teaching that a single amino acid change within an epitope, or an amino acid change outside an epitope, were both associated with the loss of subtype specificity) (Abstract attached as Exhibit 3). Clearly, antibodies raised against a protein with more than half of the amino acids being different from SEQ ID NO:10 would not necessarily bind to the protein of SEQ ID NO:10, when as little as a single amino acid change can destroy binding.

The Examiner states that "[a]nti-24P4C12 antibodies that specifically bind epitopes in the 398-710 amino acid region of 24P4C12 will also specifically bind SEQ ID NO: 10 because this region of 24P4C12 is identical to amino acids 34-321 of SEQ ID NO: 10." *Office Action* at 8 (emphasis added). Whether this statement is true or not is irrelevant because according to the Examiner, Afar generically discloses an antibody to 24P4C12, and does not disclose "antibodies that specifically bind epitopes in the 398-710 amino acid region of 24P4C12." *Office Action* at 7.

Nor has the Examiner provided any rationale based on Afar's disclosure to make antibodies to only amino acids 398-710 of 24P4C12. The Examiner cites to disclosure in Afar to assert that regions of the 24P4C12 protein that show immunogenic structure as well as other regions and domains can be identified using methods known in the art, including Kyte-Doolittle, and the Examiner includes a Kyte-Doolittle plot of 24P4C12. *Id.* at 7-8. However, the plot makes clear that there are hydrophilic regions throughout the entire length of 24P4C12, including amino acids 1-397. Therefore, the Kyte-Doolittle plot does not provide any basis for choosing to make antibodies only to amino acids 398-710 of 24P4C12. As such, antibodies to 24P4C12 do not necessarily bind to SEQ ID NO:10, since 56% of 24P4C12 differs from SEQ ID NO:10.

In sum, Afar does not disclose any antibodies to any specific region of 24P4C12. Instead, there is merely a generic disclosure of antibodies to 24P4C12. While it is possible that an antibody to 24P4C12 would bind the polypeptide of SEQ ID NO:10, it is not a certainty since more than half of 24P4C12 apparently bears no similarity to SEQ ID NO:10. Mere possibility is not sufficient for inherent anticipation: "Inherency, however, **may not be established by probabilities or possibilities.** The mere fact that a certain thing **may** result from a given set of circumstances **is not sufficient.**" *M.P.E.P.* §2112 ¶IV (8th ed. 2004), quoting *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (emphasis added). In light of the above, Applicants respectfully request that the Examiner reconsider and withdraw the 35 U.S.C. § 102(e) rejection of claims 1-5 over Afar *et al.*

35 U.S.C. § 103(a) – Afar *et al.*

In addition to the rejection of the pending claims under 35 U.S.C. § 102(e) over Afar *et al.*, the Examiner alternatively rejects the claims under 35 U.S.C. § 103(a). The Examiner argues that "[a]lternatively, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to identify hydrophilic regions in the 24P4C12 structure and to make anti-24P4C12 antibodies that recognize the hydrophilic regions, with a reasonable expectation of success." *Office Action* at 8. The Examiner then repeats his argument that "[a]nti-24P4C12 antibodies that specifically bind epitopes in the 398-710 amino acid region of 24P4C12 will also specifically bind SEQ ID NO: 10 because this region of 24P4C12 is identical to amino acids 34-321 of SEQ ID NO: 10." *Id.* Finally, the Examiner argues that "[o]ne of skill in the art would be motivated to make this modification in order to detect 24P4C12 in prostate samples. The invention is prima facie obvious over the prior art." *Id.* at 8-9. Applicants respectfully traverse.

To establish a prima facie case of obviousness, the Examiner must establish that the cited reference teaches or suggests each and every element of claimed subject matter. For the reasons discussed above, Afar does not teach each and every element of the claims, either expressly or inherently. As noted above, Afar generically discloses an antibody to 24P4C12, and does not disclose "antibodies that specifically bind epitopes in the 398-710 amino acid region of 24P4C12." *Office Action* at 8.

Even if it is obvious to make antibodies to hydrophilic regions, as discussed above, the Kyte-Doolittle plot makes clear that there are hydrophilic regions throughout the entire length of

24P4C12, including amino acids 1-397. Therefore, the Kyte-Doolittle plot does not provide any basis for choosing to make antibodies only to amino acids 398-710 of 24P4C12. As such, antibodies to 24P4C12 do not necessarily bind to SEQ ID NO:10, since 56% of 24P4C12 differs from SEQ ID NO:10.

Finally, the Examiner states that "[o]ne of skill in the art would be motivated to make this modification in order to detect 24P4C12 in prostate samples." *Office Action* at 8-9. Applicants are unclear what the Examiner means by "modification," but to the extent the Examiner is referring to making antibodies exclusively to amino acids 398-710 of 24P4C12, this statement is without support.

Applicants respectfully request that the Examiner provide evidence to support this assertion, as Applicants believe that one of skill in the art would not recognize a motivation to make antibodies exclusively to amino acids 398-710 of 24P4C12 based on the cited reference and Kyte-Doolittle plot. The Examiner's unsupported assertion of fact represents a statement by "official notice." *See, e.g., In re Zurko*, 258 F.3d 1379, 1385, 59 USPQ2d 1693, 1697 (Fed. Cir. 2001); and *In re Ahlert*, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970). Applicants submit that the Examiner's statement asserted by official notice is not well-known or capable of instant and unquestionable demonstration as being well-known. To the contrary, one of skill in the art would conclude that the plot clearly shows hydrophilic regions throughout the entire length of 24P4C12, including amino acids 1-397. Thus, in accordance with M.P.E.P. §2144.03C, Applicants respectfully request documentary evidence demonstrating that one of skill in the art would recognize a motivation to make antibodies exclusively to amino acids 398-710 of 24P4C12 based on the cited reference and Kyte-Doolittle plot. If this is not what was meant by the Examiner's statement that "[o]ne of skill in the art would be motivated to make this modification," Applicants request that the Examiner clarify to what "modification" he is referring.

A generic disclosure of antibodies to an entire protein is not a disclosure of antibodies to a specific region. Absent some motivation to make antibodies exclusively to amino acids 398-710 of 24P4C12, the disclosed antibodies to 24P4C12 clearly do not inherently possess the claimed features. Because the cited reference does not disclose each and every element of the claims, either expressly or inherently, the Examiner has failed to establish a prima facie case of

obviousness. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-5 under 35 U.S.C. § 103(a) as obvious over Afar *et al.*

CONCLUSION

In view of the above, Applicants respectfully maintain that claims are patentable and request that they be passed to issue. Applicants invite the Examiner to call the undersigned if any remaining issues may be resolved by telephone.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 9/12/07

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